III. REMARKS

A. Status of the Claim

Claims 1, 3, 5, 7, 8, 12, 13, 22 and 23 were amended without prejudice or admission.

New claims 37-40 were added.

Support for "an analgesically effective amount" in claims 1 and 3 can be found, e.g., in paragraph [0012] of the specification.

Support for "microemulsion" in claims 1, 7 and 8, and "emulsion" in claim 37 can be found, e.g., in paragraphs [0059] to [0066] and Example 3 of the specification.

Support for "the opioid antagonist is not releasable from the transdermal delivery device applied topically intact to a skin of a human patient, and is releasable from the transdermal delivery device administered intraoraly" in claim 1, and for "the opioid antagonist is not releasable from the transdermal delivery device applied topically intact to a skin of a human patient, and is releasable from the transdermal delivery device which is administered intraoraly, chewed, soaked, punctured, or torn" in claims 3 and 39 can be found, e.g., in paragraphs [0012], [0020] and [0024] of the specification.

Support for "multiphasic polymeric microspheres in which the opioid antagonist is dispersed in oily droplets in polymeric matrix" in claim 5 can be found, e.g., in paragraph [0062] of the specification.

Support for "a copolymer of poly(e)caprolactone or a poly(orthoester)" in claim 39 and "poly(e)caprolactone" in claim 40, can be found, e.g., in paragraphs [0051] and [0053] of the specification. Applicants respectfully note that "poly(e)caprolactone" and poly(orthoester) are polyesters and are encompassed by the elected species of "copolymers of polyesters."

Claims 1-13, 18-19, 21-23, 31-32, and 37-40 are currently pending, and encompass the elected species.

It is respectfully submitted that no new matter has been added by virtue of the present amendments.

B. Substance of Interview

Applicants hereby make of record the substance of the telephone interview conducted on October 14, 2010, between the undersigned attorney and Examiner Kevin S. Orwig and Primary Examiner Lakshmi Channavajjala.

During the interview, the proposed claim amendments filed on September 20, 2010, were discussed in view of US 5,149,538 to Granger et al., US 2002/0100127 to Oshlack et al., US. 2003/0068392 to Sackler, and U.S. 2004/0013716 to Gale et al..

The Examiner indicated that the proposed amendments would overcome the art of record, but may not be sufficient to place the claims in conditions for allowance, because, according to the Examiner, there may be references disclosing microspheres comprising microemulstion (e.g., U.S. 5,288,502 to McGinity, mentioned in the present specification).

Applicants submitted that the '502 patent was not reviewed in preparation for interview, but will be reviewed prior to responding to the next Office Action. Applicants now reviewed the '502 patent and submit that there is simply no disclosure in the '502 of microspheres comprising an opioid antagonist or a suggestion that microspheres comprising an opioid antagonist may be dispersed in an opioid agonist containing layer of a **transdermal delivery device** as recited in instant independent claims 1 and 3.

The Examiners indicated that amending present independent claims to specify the polymer of the claimed microspheres may further distinguish the present claims from the cited references and may expedite allowance.

Applicants thank the Examiners for their suggestion and note that the proposed amendments (i.e., amending claim 1 to recite that the microspheres comprise "a microemulsion of an opioid antagonist"), as well as some additional amendments (e.g., amending claim 3 to recite that the microspheres comprise (i) an opioid antagonist, (ii) a polyester copolymer of lactic and glycolic acid and (iii) calcium chloride) are being made in the present response.

Applicants respectfully request that the Substance of Interview is made of record and invite the Examiner to contact the undersigned at the telephone number provided below to resolve any outstanding issues.

C. Information Disclosure Statement

The Office Action recites that "[r]eferences lined-through on the information disclosure statement(s) were not considered because they were not provided, were not provided in English, or did not have a proper publication date." Office Action, page 2.

Applicants respectfully note that Form PTO-1449s returned with the Office Action did not contained any references which were lined-through, and respectfully request that the Examiner confirms that all of the references listed on the returned Form PTO-1449s were considered.

D. Abstract

The Abstract of the disclosure was objected to. The Examiner states on page 3 of the Office Action that "[a] new abstract (150 words or less) is required that is sufficiently

detailed as to provide general information about the precise nature of the invention to which the claims are directed."

In response, Applicants submit herewith a replacement abstract. The replacement abstract recites: "Abuse resistant opioid transdermal delivery device containing opioid antagonist microspheres dispersed in an opioid agonist containing layer." Support for the replacement abstract can be found, e.g., in original claim 1.

Withdrawal of the objection is respectfully requested.

E. Claim Rejections- 35 U.S.C. § 112 (2nd paragraph)

Claims 1 and 3 (and the claims dependent thereon) were rejected under 35 U.S.C. § 112, second paragraph, for reciting "an effective amount."

Claims 1 and 3 were amended to recite "an analgesically effective amount."

Withdrawal of the rejection is respectfully requested.

Claim 22 was rejected under 35 U.S.C. § 112, second paragraph, for reciting "rubber-like."

Claim 22 was amended to delete "rubber-like."

Withdrawal of the rejection is respectfully requested.

F. Claim Rejections- 35 U.S.C. § 102

Claims 1, 5, 8, 12, 13, 18, and 21 were rejected under 35 U.S.C. § 102(b) as anticipated by U.S. 5,149,538 to Granger et al. ("The Granger patent").

The rejection is respectfully traversed.

Independent claim 1, the only independent claim included in the present rejection, is directed in part to a transdermal delivery device comprising microspheres "which are visually indiscernible."

Applicants respectfully submit that there is no description of microspheres "being visually indiscernible" in the Granger patent as recited in claim 1.

In an effort to advance prosecution and to further differentiate over the Granger patent, claim 1 was amended to recite that the claimed microspheres comprise "a microemulsion of an opioid antagonist." Applicants respectfully submit that there is no description of microspheres comprising "a microemulsion of an opioid antagonist" in the Granger patent, and that the device of the instant claim 1 is structurally distinct from the devices of the Granger patent.

Claim 1 was further amended to recite that "the opioid antagonist is not releasable from the transdermal delivery device applied topically intact to a skin of a human patient, and is releasable from the transdermal delivery device administered intraoraly." The Granger patent purports "to prevent release of the antagonist **unless** the dosage form is ingested or immersed in water, alcohol or other solvent." *See e.g.,* column 2, lines 44-46 (emphasis added). With respect to the immersion in water, the Granger patent states that the antagonist is released when the device is "... **substantially** immersed in water or other solvents." See, e.g., column 2, lines 1-2, and lines 44-45; see also column 5, 30-31, and claim 7. Applicants therefore submit that the Granger patent does not teach a transdermal delivery device wherein the antagonist is "releasable from the transdermal device administered **intraoraly**" as recited in amended claim 1, as intraoral administration does not constitute "substantial" immersion in water.

For the foregoing reasons, Applicants submit that claim 1 and claims 5, 8, 12, 13, 18 and 21 which depend from claim 1 are not anticipated by the Granger patent, and request withdrawal of the rejection.

G. Claim Rejections- 35 U.S.C. § 103

Claims 2-4, 6, 7, 9-11, 19, 22, 23, 31, and 32 were rejected under 35 U.S.C. § 103(a) over the combination of the Granger patent and U.S. 2004/0013716 to Gale et al. ("the Gale publication"). The Gale publication was relied upon by the Examiner for the teaching of mean diameter of particles described therein.

The rejection is respectfully traversed.

Independent claim 3, the only independent claim included in the present rejection, is directed in part to a transdermal delivery device comprising opioid antagonist microspheres dispersed in a layer of an opioid agonist.

Applicants respectfully submit that the combination of the cited references would not have suggested to a skilled person "a transdermal delivery device comprising opioid antagonist microspheres dispersed in a layer of an opioid agonist," because the Gale publication teaches to separate the antagonist containing layer from the agonist containing layer, e.g., by a barrier layer. *See e.g.* Figures 1-5; see also paragraphs [0016], [0017], and [0022].

In an effort to advance prosecution and further differentiate from the disclosure of the cited references, claim 3 was amended to recite that the claimed microspheres comprise "(i) an opioid antagonist, (ii) a polyester copolymer of lactic and glycolic acid and (iii) calcium chloride."

Applicants respectfully submit that the combination of the cited references does not provide a reason for the skilled person for formulate microspheres "comprising (i) an

opioid antagonist, (ii) a polyester copolymer of lactic and glycolic acid and (iii) calcium chloride," and to disperse such microspheres in an opioid agonist containing layer of a transdermal delivery device as recited in claim 3.

Applicants therefore submit that claim 3 is not rendered obvious by the combination of the cited references.

With respect to claims 2, 4, 6, 7, 9-11, 19, 22, 23, 31, and 32, Applicants respectfully submit that these claims defend from claim 1 and are not rendered obvious by the combination of the cited reference for the reasons given above with respect to the anticipation rejection of claim 1.

Withdrawal of the rejection is respectfully requested.

H. Double Patenting

1. U.S. Patent Application No. 10/476,601

Claims 1-13, 18, 19, 21-23, 31, and 32 were provisionally rejected under the judicially created doctrine of obviousness-type double patenting over claims 1, 2, 32, and 33 of copending application No. 10/476,601, in view of the Granger patent and the Gale publication.

The rejection is traversed.

Applicants submit that, at the very least, the claims of the '601 application do not recite "microspheres comprising a microemulsion of an opioid antagonist and being visually indiscernible in the drug containing layer" as recited in instant claim 1, and microspheres "comprising (i) an opioid antagonist, (ii) a polyester copolymer of lactic and glycolic acid and (iii) calcium chloride" as recited in instant claim 3; and the Granger

patent and the Gale publication do not cure these deficiencies for the reasons given above in response to the anticipation and obviousness rejections.

Withdrawal of the provisional rejection is respectfully requested.

2. U.S. Patent Application No. 11/865,387

Claims 1-13, 18, 19, 21-23, 31, and 32 were provisionally rejected under the judicially created doctrine of obviousness-type double patenting over claims 1-33 of copending application No. 11/865,387, in view of the Granger patent and the Gale publication.

Applicants submit that, at the very least, the claims of the '387 application do not recite "microspheres comprising a microemulsion of an opioid antagonist and being visually indiscernible in the drug containing layer" as recited in instant claim 1, and microspheres "comprising (i) an opioid antagonist, (ii) a polyester copolymer of lactic and glycolic acid and (iii) calcium chloride" as recited in instant claim 3; and the Granger patent and the Gale publication do not cure these deficiencies for the reasons give above in response to the anticipation and obviousness rejections.

Withdrawal of the provisional rejection is respectfully requested.

IV. Conclusion

An early and favorable action on the merits is earnestly solicited. The Examiner is respectfully invited to contact the undersigned at the telephone number provided below if he believes that a telephonic interview will advance the prosecution of the present application.

Respectfully submitted,
DAVIDSON, DAVIDSON & KAPPEL, LLC

By: _____
Oleg Ioselevich
Reg. No. 56,963

Davidson, Davidson & Kappel, LLC
485 Seventh Avenue, 14th Floor
New York, New York 10018
(212) 736-1940

ABSTRACT

Abuse resistant opioid transdermal delivery device containing opioid antagonist microspheres dispersed in an opioid agonist containing layer.